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ABSTRACTS

Cancer Patients

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SUSCEPTILBILTY PROFILE OF 288 *Streptococcus pneumoniae* IN PATIENTS WITH CANCER (1998—2002)

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BACKGROUND: The rise in community acquired multidrug-resistant (MDR) *Streptococcus pneumoniae* has posed a serious challenge in the selection of appropriate antimicrobials for effective prophylaxis and empiric-preemptive treatment of susceptible patients with cancer. The frequency of drug-resistance in clinical *S. pneumoniae* isolates in patients receiving cancer therapy is not certain.
METHODS: All consecutive clinical isolates of *S. pneumoniae* between January 1, 1998 and December 31, 2002 were analyzed. *In vitro* antimicrobial susceptibility was performed according to NCCLS guidelines; isolates with MICs $>1\,\mu g/ml$ for penicillin (PCN) and $\geq 2\,\mu g/ml$ for ceftriaxone (CTX) were considered resistant (R).
RESULTS: During these 5 years, 141 (49%) of 288 total isolates were from blood culture samples; 110 (38%) respiratory samples included sputum, bronchial wash and lavage. Susceptibility to penicillin: 135 (47%) isolates were susceptible; in 151 non-susceptible *S. pneumoniae*, 68% ($n = 102$) showed MIC in resistant range. Ceftriaxone susceptibility: 91% ($n = 262$) were susceptible, and all except one isolate, among 24 non-CTX susceptible *S. pneumoniae* were in the intermediate range ($n = 23$). Yearly susceptibility trends of blood and respiratory tract isolates are presented in Table below.
CONCLUSIONS: In sharp contrast to drug-resistance profiles of S. pneumoniae isolated from general population, it was unexpected to find that most PCN non-susceptible strains for cancer patients were resistant rather having intermediate susceptibility. The decline in PCN resistance after the year 2000 may in part reflect widespread use of anti-streptococcal fluoroquinolones in patients receiving treatment for cancer.

Specimens	1998	1999	2000	2001	2002
Blood	$N = 22$	$N = 37$	$N = 30$	$N = 32$	$N = 20$
PCN-S	14 (64%)	15 (42%)	12 (40%)	18 (56%)	13 (65%)
PCN-I	0	1 (3%)	4 (13%)	6 (19%)	6 (30%)
PCN-R	8 (36%)	20 (56%)	14 (47%)	8 (25%)	1 (5%)
CTX-S	22 (100%)	37 (100%)	28 (93%)	26 (81%)	18 (90%)
CTX-I	0	0	2 (7%)	6 (19%)	2 (10%)
CTX-R	0	0	0	0	0
Respiratory	$N = 4$	$N = 13$	$N = 24$	$N = 27$	$N = 42$
PCN-S	2 (50%)	5 (38%)	8 (33%)	13 (48%)	19 (46%)
PCN-I	0	1 (8%)	1 (4%)	9 (33%)	14 (34%)
PCN-R	2 (50%)	7 (54%)	15 (63%)	5 (19%)	8 (20%)
CTX-S	3/3 (100%)	12/12 (100%)	23 (96%)	23 (85%)	36 (86%)
CTX-I	0	0	1 (4%)	3 (11%)	6 (14%)
CTX-R	0	0	0	1 (4%)	0

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CHANGING SPECTURM OF POST-VIRAL PNEUMONIA IN HOSPITALIZED PATIENTS WITH CANCER

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BACKGROUND: Influenza and respiratory syncytial virus (RSV) infections are associated with increased host's susceptibility for secondary bacterial superinfections. *Streptococcus pneumoniae*, *Staphylococcus aureus*, including emerging community-acquired methacillin-resistant strains, and occasionally gram-negative bacilli may lead to often serious, necrotizing pneumonia. We present a changing spectrum of post-viral pulmonary superinfection in our cancer patients during 2003.
RESULTS: **Case 1**. A 55-year-old neutropenic man planned to undergo allogeneic hematopoietic stem cell transplantation (HSCT) for CLL was responding favorably to ribavirin (2 gram daily) therapy for RSV infection. A black facial lesion appeared 6 days post-transplant; in next 72 hours more than 15 pleomorphic ecthyma gangrenosum-like skin lesions developed predominantly on his extremities, and the bilateral pleural-based pulmonary infiltrates were highly suggestive of invasive fungal disease. Blood cultures were sterile, albeit, *Fusarium* spp. was isolated from bronchoalveolar lavage and skin biopsy samples. Disseminated fusariosis was fatal in this patient with prior ($\sim$4 week) known nasopharyngeal *Fusarium* spp. colonization. **Case 2**. A 4-year-old boy was being treated with 6-mercaptopurine and intrathecal baclofen for refractory ALL and had responded favorably to rimantadine plus oseltamivir for influenza infection. A week after antiviral therapy was discontinued he developed intermittent fever, hypoxemia, and new multicentric pulmonary infiltrates. Tracheal aspirate and blood culture reveal multidrug-resistant *Pseudomonas aeruginosa*, which responded to combination antimicrobial therapy. The *P. aeruginosa* isolated during infection was pheotypically identical to the respiratory tract and tracheostomy site colonizing strain ($>$4 weeks).
CONCLUSIONS: In immunosuppressed cancer patients with respiratory tract bacterial and/or fungal colonization appears to alter the spectrum of post-viral pulmonary superinfection.

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VANCOMYCIN-TOLERANT NON-ENTEROCOCCAL GRAM-POSITIVE BACTEREMIA—AN EMERGNG PHENOMENON IN PATIENTS WITH CANCER

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BACKGROUND: Emergence of vancomycin-tolerant gram-positive bacterial infection, poses yet another treatment challenge. The impact of this microbiological phenomenon on clinical outcomes in the immunosuppressed cancer patients is uncertain.
METHODS: Eight patients with non-enterococcal gram-positive bloodstream infection who failed to respond to vancomycin therapy were further evaluated between 1993 and 2003. The organism identification and minimum inhibitory concentration (MIC) and minimum bactericidal concentration (MBC) were performed at the Infectious Diseases Research Laboratory at MDACC by methods outlined by National Committee on Clinical Laboratory Standards (NCCLS).
RESULTS: Please refer to the **Table** below. All eight patients had persistent bacteremia ($\geq$72 h) after institution of vancomycin. An indwelling intravascular catheter (IC) was present in all, although there was no clinical or microbiologic (IC tip culture) evidence of catheter infection. In patients 1 to 5, IC was removed $\leq$48 h after initial blood culture report became available. Similarly a secondary focus of infection was not present. In 3 patients (2, grade II-III, and 5, 6 Grade III-IV) oral mucosal excoriation was present. In patients 1 to 4, gentamicin (3 to 5 mg/kg daily) plus rifampin (600 mg daily) and in patients 5 to 8, gentamicin alone lead to a rapid ($\leq$24 h) improvement as fevers abate and blood cultures became sterile. No infection recurrence occurred after discontinuation of 10 to 14 days of parenteral combination antimicrobial therapy.
CONCLUSIONS: Vancomycin-tolerant gram-positive bacteremia was seen sporadically during the past decade at this comprehensive cancer center. Awareness and prompt addition of adjuvant aminoglycoside and/or rifampin was associated with a favorable response in these high-risk cancer patients.

Pt.	Age, sex	Cancer	ANC	Microorganisms	MIC	MBC
1	55 y, F	Ovarian, metastatic	300	*Staphylococcus aureus*	0.25	32
2	60 y, M	AML	100	*Staphylococcus aureus*	1	64
3	42 y, F	Breast, autologous SCT	450	*Staphylococcus epidemidis*	2	128
4	44 y, M	Kaposi's sarcoma, AIDS	300	*Streptococcus*, gp G	0.25	16
5	38 y, F	Breast, autologous SCT	<100	*Streptococcus mitis*	0.5	32
6	37 y, F	AML	<100	*Streptococcus sanguis*	0.12	32
7	44 y, M	Sarcoma, metastatic	5000	*Staphylococcus aureus*	1	128
8	68 y, F	Malignant melanoma	2000	*Streptococcus* gp G	0.12	32

NOTE. SCT: Stem cell transplant. AML: Acute myelogenous leukemia. MIC, and MBC values are given in micrograms per milliliter. ANC: Absolute neutrophil count is given in cells/mm^3.

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INFECTIONS IN PATIENTS WITH BILIARY OBSTRUCTION DUE TO PANCREATIC AND HEPATOBILIARY CANCER: LONG TERM FOLLOW-UP

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OBJECTIVE: To analyse episodes of fever, their nature and management, in patients with hepatobiliary and pancreatic carcinoma with biliary drainage, and to evaluate the correlation between biliary isolates and other documented infections.
METHODS: A retrospective analysis of all episodes of fever in 122 patients with hepatobiliary and pancreatic carcinoma that required biliary drainage, between January 2000 and December 2001, was performed. Episodes were subdivided into early follow-up (since the insertion of the drainage until surgery), post-operative (those occurring in the 30 days following surgery) and long term follow-up (those that occurred thereafter).
RESULTS: Fever was the most frequent complication in all the periods of follow-up, representing almost always a documented infection. Cholangitis was the most frequent infection during the early and long-term follow-up. Ninety-nine patients underwent surgery. 54% had one or more infection complications, wound infection and abdominal collection being the most frequent. Febrile neutropenia was an infrequent complication, requiring prompt decompression through the insertion or change of the stent or transhepatic catheter, and/or a short course of antibiotics. In 24 cases there were paired samples of biliary fluid and a documented infection in 19 cases one or more of the biliary isolates were also isolated from the documented infection Diverse species of Candida were frequently isolated from biliary culture with no documented increased risk of invasive fungal infection in these patients.
CONCLUSION: In this population of patients with obstruction of the biliary tree fever was the most frequent complication and almost always represented a documented infection. There was a good correlation between biliary isolates and other documented infections.

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ANTIMICROBIAL RESISTANCE OF GRAM-NEGATIVE BACTERIA IN A CANCER HOSPITAL

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OBJECTIVE: The aim of the trial was studying the rate of *Pseudomonas aeruginosa* resistance and rate of ESBL − producers in cancer patients with nosocomial infections in ICU compared with surgical departments.
METHODS: Seventy one strains of *P. Aeruginosa* and 127 strains with a probability of ESBL producing isolated in X-202−III-2003, were analyzed. Identification and susceptibility testing was performed with ATB-Expressions (BioMerieux, France).
RESULTS: 27 of 71 (38.0%) of *P. aeruginosa* strains were resistant to various antimicrobials. Resistance to ciprofloxacin was 68% in SD vs. 87% in ICU ($p>0.05$); resistance to tobramycin, amkacin, gentamycin was 61%, 59%, 63% in SD vs. 87%, 81%, 87% in ICU, respectively ($p>0.05$). Resistance to ceftazidime and cefepim was 30% and 26% in SD vs. 71% and 57% in ICU, respectively ($p < 0.001-0.02$). Resistance to piperacillin-tazobactam and ticarcillin-clavulanate was 33% and 44% in SD vs. 53% and 70% in ICH, respectively, ($p < 0.05$), resistance to imipenem and meropenem was 26% & 34% in SD vs. 71% and 73% in ICU, respectively ($p < 0.01-0.1$). Eleven (15.5%) of *P. aeruginosa* strains, isolated from different patients were resistant to all tested antimicrobials (6 in ICU, 5 in SD). In ICU only 8 strains of *Enterobacteriaceae* were isolated including *E. coli* −4, *Klebsiella spp.* −3 and *Proteus spp.* −1 be-

cause of non-fermenting rods prevalence. Among 119 strains from SD, *E. coli* was identified in 81 (68.1%), *Klebsiella spp* in 26 (21.8%), *Proteus spp* were found in 1/8 (12.5%) strains in the ICU vs 2/12 (16.7%) in SD ($p < 0.05$). ESBL-producing *Klebsiella spp* were found in 0/3 (0%) in ICU vs. 8/326 (31%) in SD ($p < 0.02$), probably because of extensive prescribing of III-generation cephalosporins in SD.
CONCLUSION: Isolation of ESBL − producers and multi-resistant stains of *P. aeruginosa* requires the development of rational approaches to empirical treatment. Reduction of III generation cephalosporins utilization is needed to avoid increase of ESBL-producing Enterobacteriaceae.

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CATHETER-RELATED VANCOMYCIN-RESISTANT *Enterococcus faecium* BACTEREMIA: CINICAL AND MOLECULAR EPIDEMIOLOGY

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To study the clinical and molecular epidemiology of vancomycin resistant *Enterococcus faecium* (VREF) organisms causing catheter-related bacteriemia (VREF-CRB), ten patients with VREF-CRB were compared to 30 control patients with gastrointestinal colonization by VREF. Patients with VREF-CRB were more likely to have required mechanical ventilation (<0.01), received total parenteral nutrition ($P < 0.01$), and had polyurethane catheters ($P < 0.01$) inserted in the femoral vein ($P = 0.01$). Using pulsed field gel electrophoresis, four of the ten VREF-CRB isolates were genetically indistinguishable, whereas only two of the 30 control VREF isolates displayed this same DNA pattern ($P = 0.03$). In conclusion, VREF-CRB occurs more frequently in patients who received total parenteral nutrition, mechanical ventilation and femoral catheters.

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BLOODSTREAM INFECTIONS SURVEILLANCE IN A CANCER CENTER: A PROSPECTIVE LOOK AT CLINICAL MICROBIOLOGY ASPECTS

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OBJECTIVE: To describe the frequency of occurrence and antimicrobial susceptibility profiles of bloodstream infection (BSI) isolates at a tertiary care referral oncology center.
METHODS: A prospective clinical and microbiologic surveillance study was conducted during a 26-month period and evaluated all consecutive inpatients with malignancies or post-bone marrow transplant with positive blood cultures.
RESULTS: The study enrolled 859 episodes of BSI in 719 patients. There were 6.9 BSI episodes/1000 patient-days. Overall in-hospital mortality was 25%. Median patients' age was 43 years, 71% of episodes occurred in patients above 18 years of age. Patients with underlying hematology malignancies accounted for 38.2% of the episodes. An indwelling CVC was present in 61% of episodes. BSI origin was unknown in 27% of the episodes, associated with other sites in 49.6% and catheter-related in 23.4%. There were 638 concomitant infectious sites: lungs, 28.4%; urinary tract, 14.8% and non-surgical skin/soft tissue 9.7%. In total, 1039 microorganisms were isolated within 48 h after the first blood culture: gram-negative rods (56%). *Escherichia coli* and coagulase negative staphylococci. *Klebsiella pneumoniae* (37.8%) and *E. coli* (8.9%) produced ESBL. High rates of ceftazidime resistance were detected among *Acinetobacter* spp. (40%) and *Enterobacter* spp. (51.2%). *E. coli* and *K. pneumoniae* were frequently isolated from hematology patients and *Enterobacter* spp. from solid tumors patients. *E. coli*, *K. pneumoniae*, and *P. aeruginosa* were more often isolated from neutropenic than from non-neutropenic patients. Oxacillin resistance was detected in 18.7% of *Staphylococcus aureus* isolates.
CONCLUSION: Continuous multidisciplinary surveillance of BSIs is warranted in this high-risk group of patients in order to develop strategies for antimicrobial resistance control and treatment of infectious complications.

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A PROSPECTIVE EVALUATION OF THE EPIDEMIOLOGY, MICROBIOLOGY AND OUTCOME OF ADULT SURGICAL CANCER PATIENTS WITH BLOODSTREAM INFECTIONS

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OBJECTIVE: To describe the epidemiology and microbiology of BSIs among adult surgical patients and to determine independent factors influencing in-hospital mortality in order to identify a subgroup of surgical patients at higher risk of death.
METHODS: Prospective cohort study.
RESULTS: The study enrolled 112 consecutive episodes of bloodstream infections (BSI) in adult

surgical cancer patients during a 26-month period. Median age was 64.5 years, and crude in-hospital mortality 19.6%. The median duration from surgery to the index blood culture was 11 days and from index blood culture to death was 4.5 days. Advanced tumor disease was observed in 75% of patients, 36.6% of the patients were under intensive care and 68.7% had a central venous catheter in-place at the moment of BSI. Associated infected sites were present in 57.1% of episodes. There were 328 noninfectious comorbidities. Poor performance status, weight loss, hypoalbuminemia and ventilatory support corresponded to 67.4% of them. There was a predominance of aerobic gram-negative bacilli (62%), followed by gram-positive cocci (26.6%) and fungi (9.3%). The observed mortality rate in these organism groups was similar (23.6% vs. 15% vs. 28.6%, respectively; $P = 0.44$). Main isolated organisms were *Enterobacter* spp., coagulase-negative staphylococci, *Klebsiella* spp., *Acinetobacter* spp. and fungi. Nonfermentative strains predominated in patients with indwelling catheters. Thirty-five pathogens (30.2%) were considered resistant. There was no significant difference in the mortality rate between resistant or non-resistant sentinel organisms (20% vs. 26%, respectively; $P = 0.49$). Logistic regression analysis showed the presence of $\geq$4 comorbidities, advanced tumor, thoracic surgery, catheters retention and pulmonary infiltrates as independent predictors of mortality.
CONCLUSIONS: Medical and infection control measures addressing some of variables amenable to interventions might reduce the negative impact of postoperative infectious morbidity and mortality.

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MALIGNANCY AND TUBERCULOSIS: DATA FROM JULES BORDET INSTITUTE

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INTRODUCTION: Active tuberculosis (TB) rate is higher in cancer patients than in general population. It is possible that TB is a predisposing factor for cancer. It is well documented that malignancy and/or its treatment are predisposing factors for primary or reactivated TB. Malignancies and TB may also have similar presentation and differential diagnosis is not always easy.
OBJECTIVES: All TB cases in the past ten years were retrospectively reviewed in order to estimate the prevalence of TB between cancer patients of Jules Bordet Institute in the era of the new therapeutic modalities and compare it with that of population of Brussels.
MATERIAL AND METHODS: Using the searching engine of ''Oribase'', the electronic database of Jules Bordet Institute, we identified all cases of active TB hospitalized between July 1992 and July 2002. Atypical mycobacteriosis, AIDS patients, and patients not proved to have cancer were excluded. Active infection was considered to be present either if cultures where positive for Mycobacterium tuberculosis or if biopsy or autopsy revealed lesions highly suggestive of active tuberculosis. Patient's medical charts were reviewed for clinical and laboratory characteristics. Age, sex, clinical presentation, past history of TB, underlying malignancy and recent treatment, predisposing factors, anti TB therapy and outcome, were recorded. The yearly rate of TB in cancer patients of our Institute was also calculated and compared with the overall rate of TB in Brussels.
RESULTS: Thirty-two cancer patients with active TB were identified. This corresponds to a mean annual new case rate of all patients hospitalized in the Institute of 117,6 new cases/100.000 patients/year. The mean annual incidence of TB for the years 1993—2000 for Brussels was 35,93 cases/100.000 population/year. Three of the patients had prior history of treated TB. TB occured in 11 patients with lung cancer, 6 with ORL cancer, 4 with breast cancer, 1 with esophageal cancer, 1 with osteosarcoma, 1 with renal cell cancer, 1 with prostate cancer, 1 with endometrial carcinoma, 1 with B-cell non-Hodgkin lymphoma, 1 with MDS, 1 with CML, 1 with CLL, 1 with AML and in 1 patient with simultaneous occurrence of ORL and lung cancer. In 3 patients TB and malignancy were diagnosed simultaneously. 21 patients had been administered an antineoplastic therapy (12 patients chemotherapy, 4 radiotherapy and 5 both chemotherapy and radiotherapy) whereas no antineoplastic or other immunosupressive treatment was given in 11 cases. Culture specimens were positive in 30 cases and post mortem diagnosis was made in 2 cases. The type of infection was as follows: 27 cases of pulmonary TB, 2 cervical lymph TB, 1 mediastinal tuberculous lymphadenopathy, 1 intestinal TB and 1 of miliary TB. Mortality due to TB was 6,25% (autopsy proven).
CONCLUSIONS: Cancer patients treated in Jules Bordet Institut between 08/1992—08/2002 had a 3,27 fold risk of active TB in comparison to the general population in Brussels. Reactivation seems to be the case for the great majority of our patients. Latent tuberculosis represents an equilibrium state between host and bacillus. Immune deficiency is commonly implicated in the reactivation of TB. In

these cases the malignancy per se (e.g. lymphoproliferative disorders), or/and the therapeutic agents are responsible for the immunosuppression. Debilitation, cahexia and malnutrition, situations commonly accompanying malignancies are also well known to compromise the immune system. Though their significance is not well documented, it seems reasonable that local factors may result also in reactivation of TB. Radiation therapy may be also a predisposing factor that impairs the immune function and produces local damage. The coexistence of these two entities may create major diagnostic and therapeutic problems. So if TB or malignancy is not diagnosed, this can be misdiagnosed as dissemination of the cancer or as failure of antituberculous treatment.